

Atty Dkt. No.: SKEL-008  
USSN: 10/717,171

### **REMARKS**

In view of the following remarks, the Examiner is requested to allow Claims 1-29, the only claims pending and under examination in this application.

#### ***Claim Rejections - § 103(a)***

Claims 1-3, 10, 11, 13, 15-17, 21 and 23-25 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Chow *et al.* (USPN 5,525,148).

According to the MPEP § 706.02 (j), to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

An element of the rejected claims is an osteoclastogenic agent. The Applicants define an osteoclastogenic agent as one that induces osteoclastogenesis, i.e., an agent that causes differentiation of hematopoietic monocyte/macrophage precursors into osteoclasts. See page 6, line 30 to page 7, line 2. An osteoclast functions to resorb bone.

The conventional approach to treating bone fractures follows the principle that in order to promote bone regeneration and growth it is beneficial to recruit osteoblasts to a treatment site so as to support bone formation. Osteoblasts function by secreting enzymes that promote mineral deposition and therefore aid in the growth and development of bone. The methods set forth in Chow follow this conventional approach.

Chow is directed to methods for making hydroxyapatite forming cements. The cements disclosed by Chow may include an osteoinductive factor. Osteoinduction is a process that

Atty Dkt. No.: SKEL-008  
USSN: 10/717,171

stimulates osteogenesis or bone formation. Accordingly, the osteoinductive factors set forth in Chow function to recruit osteoblasts to the site of treatment. This is a completely different approach than the one taken by the Applicants.

The methods taught by the Applicants are contrary to the conventional approach because rather than recruiting osteoblasts to a treatment site the Applicants' methods recruit osteoclasts. The Applicants' methods, therefore, are opposite from those set forth in Chow.

In making the instant rejection the Examiner interprets the term "osteoclastogenic agent" to be synonymous with the term "osteoinductive factor." However, this interpretation is not correct. As set forth above, an osteoinductive factor is one that recruits osteoblasts. An osteoclastogenic agent is one that leads to the production of osteoclasts. Osteoclasts function to resorb bone and have a function that is opposite osteoblasts. Accordingly, osteoinductive factors and osteoclastogenic agents function in different ways and should not be considered synonymous.

Therefore, the Applicants contend that the term "osteoclastogenic agent" is not synonymous with the term "osteoinductive factor" and therefore a *prima facie* case of obviousness has not been established because Chow neither teaches nor suggests an "osteoclastogenic agent." Chow does not suggest an "osteoclastogenic agent" because Chow teaches the use of an osteoinductive factor, which has an activity that is opposite of an osteoclastogenic factor. The Applicants, therefore, respectfully request the 35 U.S.C. § 103(a) rejection of Claims 1-3, 10, 11, 13, 15-17, 21 and 23-25 be withdrawn.

Claims 1, 12, 15 and 20 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Chow *et al.* (USPN 5,525,148) in view of Constantz (USPN 6,375,935).

An element of the rejected claims is an osteoclastogenic agent. As stated above, Chow is deficient because it neither teaches nor suggests an osteoclastogenic agent. As Constantz

Atty Dkt. No.: SKEL-008  
USSN: 10/717,171

was cited solely for its disclosure of soluble silicate solutions for use in conjunction with the setting of calcium phosphate cements it fails to remedy the deficiencies of Chow. Accordingly, Chow in combination with Constantz fails to teach all the elements of the claimed invention and a *prima facie* case of obviousness has not been established. The Applicants, therefore, respectfully request the 35 USC § 103(a) rejection of Claims 1, 12, 15 and 20 be withdrawn.

Claims 1-13, 15-19, 21 and 23-25 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Chow *et al.* (USPN 5,525,148) in view of Yasuda *et al.* (Proc. Natl. Acad. Sci. USA 1998, 95, 3597-3602).

Contrary to the position of the Office, the Applicants contend that a *prima facie* case of obviousness has not been established because there is no motivation to combine the cited references in the manner suggested by the Office.

Chow discloses the use of an osteoinductive factor. As explained above, an osteoclastogenic agent is completely different from an osteoinductive factor. Chow is completely silent with respect to the use of an osteoclastogenic agent and in fact teaches use of an agent with opposite activity. Accordingly, Chow neither teaches nor suggests an osteoclastogenic agent and in fact teaches the use of an opposite type of agent.

Because Chow does not teach or suggest the use of an osteoclastogenic agent, one would not be motivated to employ the RANKL agent Yasuda in the cement of Chow.

Hence, there is no motivation to combine the cited references in the manner suggested by the Examiner and a *prima facie* case of obviousness has not been established. The Applicants, therefore, respectfully request that the 35 U.S.C. § 103(a) rejection of Claims 1-13, 15-19, 21 and 23-25 be withdrawn.

Atty Dkt. No.: SKEL-008  
USSN: 10/717,171

Claims 1, 14, 15 and 22 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Chow *et al.* (USPN 5,525,148) in view of Chow *et al.* (J. Biomed. Mater. Res. (Appl Biomater) 2000, 53, 511-517).

An element of the rejected claims is an osteoclastogenic agent. As stated above, Chow (the '148 patent) is deficient because it neither teaches nor suggests an osteoclastogenic agent. As Chow *et al.* was cited solely for its disclosure of compressive strength ranges of calcium phosphate cements it fails to remedy the deficiencies of Chow (the '148 patent). Accordingly, Chow (the '148 patent) in combination with Chow *et al.* fails to teach all the elements of the claimed invention and a *prima facie* case of obviousness has not been established. The Applicants, therefore, respectfully request the 35 U.S.C. § 103(a) rejection of Claims 1, 14, 15 and 22.

Claims 26-29 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Chow *et al.* (USPN 5,525,148) in view of Constantz (USPN 6,375,935).

An element of the rejected claims is an osteoclastogenic agent. As stated above, Chow is deficient because it neither teaches nor suggests an osteoclastogenic agent. As Constantz was cited solely for its disclosure of soluble silicate solutions for use in conjunction with the setting of calcium phosphate cements it fails to remedy the deficiencies of Chow. Accordingly, Chow in combination with Constantz fails to teach all the elements of the claimed invention and a *prima facie* case of obviousness has not been established. The Applicants, therefore, respectfully request the 35 U.S.C. § 103(a) rejection of Claims 1, 12, 15 and 20.

#### ***Double Patenting***

Claims 1, 11, 12, 15, 24, and 25 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1, 9, 11, 22, and 23 of co-pending U.S. Patent Application No. 10/900,029 in view of Chow *et al.* (USPN 5,525,148).

Atty Dkt. No.: SKEL-008  
USSN: 10/717,171

Solely in order to expedite prosecution, filed herewith is the requisite terminal disclaimer, in view of which the Applicants respectfully request this rejection be withdrawn.

Atty Dkt. No.: SKEL-008  
USSN: 10/717,171

**CONCLUSION**

The Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number SKEL-008.

Respectfully submitted,  
BOZICEVIC, FIELD & FRANCIS LLP

Date: 3-8-06

By: 

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Enclosure(s): Terminal Disclaimer over co-pending application serial no. 10/900,029

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